REMARKS/ARGUMENTS

All claim amendments are made without prejudice and do not represent an acquiescence in any ground of rejection. Reconsideration of the captioned application based on the previous amendments and following remarks is respectfully requested.

Status of the claims

Claim 7 is under examination. After entry of this amendment, claims 7, and 31-37 will be pending and under consideration.

Claim 7 is rejected under 35 U.S.C. §103(a) as being unpatentable over Condra et al. (*J. Virology*, 70:8270-76, 1996), Seki et al. (*Antiviral Chemistry & Chemotherapy*, 6:73-9, 1995), and Bakhanashvili et al (*FEBS Letters*, 391:257-262, 1996). Claim 7 has been amended to more particularly point out and distinctly claim the subject matter that Applicants regard as the invention. Applicants submit that the amendments are fully supported by the specification as filed, and no new matter is being added. For example, support for the proviso in claim 7(ii)(c)(1) is found in Table 1 on Page 20 of the originally filed application. Table 1 lists examples of commonly occurring secondary mutations appearing in clinical isolates after treatment with protease inhibitors, including L10I, M46I, L63P, V77I, and I84V.

Applicants appreciate the Examiner's acknowledgement that the list of inhibitors in the previously presented claim 7 (d) is describing conventional antiviral therapy effectiveness of which is being evaluated, rather than introducing limitations to the claimed method. Therefore, Applicants have deleted (d) from claim 7 to better serve the public notice function of the claim and to more particularly point out and claim the subject matter of the invention.

New claims 31-37 are being added to recapture the scope of the original application. The originally filed claim 7 involves the determination of one or more of the three recited nucleic acid molecules comprising mutations correlated with phenotypic resistance to one of the three types of drugs, NRTI, NNRTI, and PI, respectively. The currently amended claim 7 covers only the determination of ALL of the three recited nucleic acid molecules. To recapture the original scope, claims 31-32 are added involving the determination of a nucleic acid molecule comprising mutations correlated with the NNRTI resistance; claims 32-36 are added involving the determination of a nucleic acid molecule comprising mutations correlated with the NRTI resistance; and claim 37 is added involving the determination of a nucleic acid molecule comprising mutations correlated with the PI resistance.

Support for the new claims are found through out the originally filed application. For example, support for claims 31 and 33 is found in claim 7 as originally filed and no new matter has been added. Support for claim 32 is found in claim 8 as originally filed and no new matter has been added. Support for claims 34, 35, and 36 is found in the originally filed claims 9, 10, and 11, respectively, and no new matter has been added. Support for claim 37 is found in claim 7 as originally filed and Table 1 on Page 20 of the originally filed application, and no new matter has been added.

Considerations Under 35 U.S.C. §112

The Examiner had previously rejected claim 7 for the lack of enablement under 35 U.S.C. §112, first paragraph, see Office Actions dated December 23, 2002 and August 26, 2003. The Examiner has subsequently withdrawn the enablement rejection of the previously presented claim 7 in view of Applicants' arguments, see Office Action dated December 16, 2004. Those skilled in the art would be able to practice the currently amended claim 7 and the new claims 31-37 as well as they could with the previously presented claim 7, because these amended claims are fully supported by the originally filed claims and specification and no new matter has been added. Applicants

respectfully submit that the currently amended claim 7 and the newly added claims 31-37 have adequate written description and are enabled under 35 U.S.C. §112, first paragraph.

Considerations Under 35 U.S.C. §102

The Examiner had previously rejected claim 7 under 35 U.S.C. §102(b) as being anticipated by Condra et al., see Office Actions dated December 23, 2002 and August 26, 2003. The Examiner had also previously cited references of Seki et al. and Bakhanashvili et al., see Office Actions dated December 16, 2004. In the event that the Examiner is considering rejections under 35 U.S.C. §102(b) of the newly added claims 37, 33, and 31 based on Condra et al., Bakhanashvili et al., and Seki et al., respectively, Applicants discuss each of the references below.

Condra et al. discloses mutant HIV proteases correlated with reduced effectiveness of an antiviral therapy involving Indinavir, a PI. Condra et al. discloses two mutant HIV proteases having a combination of multiple mutations of (L10I, M46I, L63P, V77I, I84V, N88T, and I93L), and (L10I, M46I, L63P, I66V, V77I, I84V, N88T, and I93L), respectively, see Table 1, p8272. Applicants respectfully submit that Condra et al. does not anticipate claim 37, because the claim has excluded from the claim mutant HIV proteases comprising a combination of mutations L10I, M46I, L63P, V77I, I84V, and N88T.

Bakhanashvili et al. states that mutant HIV RT having an Y183F or M184L mutation has diminished sensitivity to NRTI, i.e., nucleoside analogs, see right column, P257. Applicants respectfully submit that Bakhanashvili et al. does not anticipate claim 33, because the claim does not involve a mutant HIV RT having an Y183F or M184L mutation as disclosed by Bakhanashvili et al.

Seki et al. discloses mutant HIV RTs that confer resistance to the MKC-442, a NNRTI. In particular, Seki et al. discloses a mutant HIV RT having a combination of two mutations K103R and Y181C, see Fig. 2, P75. Such a mutant HIV RT is distinct from the mutant HIV RT as listed in claim 31 (ii)(b), which has a combination of at least two

mutations 103R and 179D. Therefore, Applicants respectfully submit that Seki et al. does not anticipate claim 31.

Rejection Under 35 U.S.C. §103

The Examiner rejected the previously presented claim 7 under 35 U.S.C. §103(a) as being unpatentable over Condra et al., Seki et al., and Bakhanashvili et al., see Office Action mailed on September 12, 2005. Applicants respectfully submit that, for the following considerations, the amended claim 7 is not obvious over Condra et al., Seki et al., and Bakhanashvili et al.

Obviousness under 35 U.S.C. §103(a) is a question of law based on the following factual inquiries: 1) the scope and the content of the prior art; 2) the differences between the prior art and the claims at issue; 3) the level of ordinary skill in the art; and 4) objective evidence of secondary considerations. Graham v. John Deere Co., 383 U.S. 1, 17, 148 U.S.P.Q. 459, 567 (1966). The level of skill in the art is measured as of the time the invention was made. In re Epstein, 32 F.3d 1559 (Fed. Cir. 1994). "Obvious to experiment" is not a proper standard of obviousness. "Selective hindsight is no more applicable to the design of experiments than it is to the combination of prior art teachings. There must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure." In re Dow Chemical Co., 837 F.2d 469 (Fed. Cir. 1988).

First, the amended claim 7(c) has excluded from the claim mutant HIV proteases comprising a combination of mutations L10I, M46I, L63P, V77I, I84V, and N88T. The two 88T containing mutant HIV proteases, as disclosed by Condra et al., each has a combination of multiple mutations of (L10I, M46I, L63P, V77I, I84V, N88T, and I93L), and (L10I, M46I, L63P, I66V, V77I, I84V, N88T, and I93L), respectively. Thus, they are not covered by the amended claim 7. Because each of the two mutants has 6 or 7 additional point mutations in addition to the N88T mutation, without the knowledge learned from the Applicants' disclosure, undue experimentation is needed for an artisan to select the particular mutation, 88T, as a marker of effectiveness of an anti-HIV

therapy involving a PI. Thus, Condra et al. does not render claim 7(c) obviousness under 35 U.S.C. §103(a).

Similarly, the amended claim 7(b) has removed recitation of the 184L mutation mentioned by Bakhanashvili et al from the claim. There is no reason or suggestion by Bakhanashvili et al. that the particular mutations listed in the amended claim 7 (b) can be used as markers of effectiveness of an anti-HIV therapy involving a NRTI. Thus, Bakhanashvili et al. does not render claim 7(b) obviousness under 35 U.S.C. §103(a).

In addition, the amended claim 7 (a) lists mutations that can be used as markers of effectiveness of an anti-HIV therapy involving a NNRTI, which are neither described nor suggested by Seki et al. Seki et al. discloses that a mutant HIV RT having a combination of mutations K103R and Y181C is resistant to MKC-442, a NNRTI. This disclosure does not render obvious that HIV RT mutants such as those listed in claim 7 (a), including mutations 103H, 103S, 181V, or a combination of at least two mutations 103R and 179D, would also be resistant to a NNRTI. At best, Seki et al. may motivate an artisan to experiment with single substitutions at position 103 or 181 or combinations of a single substitution at position 103 or 181 with other mutations. There is no reason or suggestion in Seki et al. for selecting the particular HIV RT mutant listed in claim 7(a) other than the knowledge learned from the Applicants' disclosure. Thus, Seki et al. does not render claim 7(a) obviousness under 35 U.S.C. §103(a).

Because none of the mutations listed in claim 7 has been described or suggested in Condra et al., Seki et al., or Bakhanashvili et al., Applicants submit that the combination of these references does not render the amended claim 7 unpatentable. Applicants therefore respectfully request that the Examiner withdraw the rejection of the amended claims 7 under 35 U.S.C. §103(a).

Similar to the reasons presented in arguing for patentability of claim 7(c), Condra et al. does not render the newly added claim 37 unpatentable under 35 U.S.C. §103(a). Likewise, Bakhanashvili et al. does not render the newly added claim 33 unpatentable under 35 U.S.C. §103(a). Finally, for these same reasons, Seki et al. does not render the newly added claim 31 unpatentable under 35 U.S.C. §103(a).

Conclusion

Entry of the foregoing amendment is respectfully requested because the amendment is believed to place the application in condition for allowance.

Applicants respectfully submit that the amended claims are enabled under 35 U.S.C. §112, first paragraph, because the Examiner has deemed the previously presented claim 7 enabled and the amended claims are fully supported by the originally filed claims and the specification and no new matter has been added.

Applicants respectfully submit that the amended claims are not anticipated under 35 U.S.C. §102(b) by the references of Condra et al., Seki et al. and Bakhanashvili et al., because neither of the references has disclosed the particular HIV mutants listed the amended claims.

Applicants further submit that the amended claims are not unpatentable under 35 U.S.C. §103(a) over Condra et al., Seki et al., and Bakhanashvili et al., because neither of the references has disclosed or suggested to use the particular HIV mutants listed the amended claims. Therefore, Applicants respectfully request that the Examiner withdraw the rejection of the amended claim 7 under 35 U.S.C. §103(a).

Applicants submit that the application is in condition for allowance, and respectfully request that a timely Notice of Allowance be issued in this case.

Should the Examiner have any questions or concerns regarding the present response, he/she is invited to contact the undersigned at the telephone number provided below.

Respectfully Submitted,
/Myra H. McCormack/

Myra H. McCormack

Docket No. VIP0004USA
Attorney for Applicants
Reg. No. 36602

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-6932
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